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EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/218,277	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,9,11-13 and 16-20* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *3-7,9, 13 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *3-7,9,11-13 and 16-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 9, 11-13, 16-20 to the extent of the non-elected invention.

Continued Prosecution Application

1. The request filed on 2-24-03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/218277 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant's CPA papers were filed without further amendment or argument in response to the Office Action of 10-22-02. Therefore, the previous Office Action is repeated and made Final herein.

3. Claims 3-7, 9, 11-13 and 16-20 are pending.

4. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

5. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, applicant's continued traversal of the Restriction requirement set forth in Paper No. 13, mailed 8-15-00 and Paper No. 23, mailed 12-27-01 appears moot as the restriction requirement was made final in Paper No. 15, mailed 12-15-00. If applicant wishes to pursue the matter further they should file a petition in accordance with 37 CFR 1.144.

However, to further clarify the record applicants response 3-5-01 states that the examiner has maintained the restriction in that the claims of Group I and Group II achieve different effects as claimed, may be differently classified and require different searches. Applicants continued traversal states that the examiner is incorrect in stating that the two groups as claimed in claim 16 are separable in that they achieve different effects as claimed. This argument is based on applicant's rewording of claim 16 such that the methods of Group I and Group II are now recited together in a single claim. Applicants further contend that as claim 16 is a valid generic claim,

both groups and all species must be examined once the generic claim is found allowable.

In response the examiner notes that applicants newly presented claim 16 in fact recites the method of Group I and Group II in a single claim. However such recitation does not negate the fact that the claim is separable as defined in the restriction of 8-15-00. The different methods achieve different effects, may be differently classified and require different search and examination considerations. A reference for one would not necessarily be a reference for the other. The two methods are drawn to 1) preventing or inhibiting axonal degeneration and 2) promoting nerve regeneration. The methods are separable as evidenced by the following literature references which establish a separate status in the art of axonal regeneration and axonal degeneration which are diametrically opposed processes and are patentably distinct as evidenced by Plata-Salaman et al., (1991) Peptides 12(3):653-63, George et al., (1995) J. of Neuroscience 15(10):6445-52, Petrovich et al., (1997) 19(5):551-4, Bradbury et al., (1998) Eur. J. of Neurosci., 10(10):3058-68, Pan et al., (1997) Neurosci. & Biobehav. Reviews 21(5):603-13 and Wang et al., (2000) J. of Neuropath. & Exp. Neurol., 59(7):599-606. The methods may be separately classified for example in class 435, subclasses 374, 375 or 377. The search and examination of both groups together represents a burden to the examiner, regardless of any similarity in reagents or steps. Thus, it is further noted that as such the claim is not properly generic as the methods do not share the characteristics of a genus, i.e., a common utility or function. Alternatively, the claims define distinct methods with different use, different modes of operation, different function and different effects, see in particular MPEP 803.02 and 806.04. It is also noted that no claim is indicated allowable and thus applicants are not presently entitled to the search and examination of any other group or species of the claimed invention.

Applicants response of 12-27-01 further argues that the preamble statement "preventing or inhibiting axonal degeneration and/or promoting nerve regeneration" is a statement of intended mechanism, that whatever happens, happens whether it is stated in the preamble of the claim or not and that anyone administering the composition to a person having such a defined injury or disease will inherently achieve prevention or inhibition of axonal degeneration and/or promotion of nerve regeneration. Applicants further argue that issuance of two patents to such delimited claims would constitute issuance of two patents to the same invention.

In response to applicant's arguments filed 12-27-01, it is noted that the claim recitations noted by applicant's are within the preamble of the claim and thus obtain consideration as patentable weight. Thus a reference to one mechanism would not necessarily encompass (under 35 USC 102 and 103) the other. Applicant's do not appear to be conceding the point that a reference to inhibiting axonal degeneration, for example, would render promoting nerve regeneration, obvious. In any case, the generic claim is not deemed allowable or free from the prior art. Upon the determination of allowable subject matter, the Examiner would reconsider rejoinder depending upon the terms of the claims.

Again, the requirement is still deemed proper and is therefore made FINAL.

6. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 9-13, and 16-19 in part are withdrawn as set forth in Paper No's 15 and 19 from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The elected species is to a method of delivering antigen, specifically Myelin Basic Protein antigen of SEQ ID NO:12. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

7. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, newly submitted claim 20 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 20 appears to be a substantial duplicate of canceled claim 10. The claim is withdrawn to the extent of the nonelected invention, for the same reasons of record as set forth above for claim 10, the combination/sub-combination being separable and the elected invention being limited to the extent of the MBP antigen as set forth above.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 20 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections

8. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 3-7, 9, 13, and 16-20 stand objected to under 37 CFR 1.75(c), as being drawn to nonelected subject matter and thus to multiple, patentably distinct inventions.

Applicant's argue as set forth above that the inventions are not patentably distinct. In paper No. 28, 7-29-02 applicant's further argue that the groups are not so diverse as to create an improper Markush group, that the species should be examined once found allowable and that the objection should be held in abeyance until such determination.

Applicant's arguments filed 12-27-01 have been fully considered but are not persuasive as set forth above. The inventions are drawn to multiple patentably distinct inventions with different methods, reagents, steps, outcomes and mechanisms, in particular, M.P.E.P. 803.02

states that:

"Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

Applicant's arguments filed 7-29-02 have also been fully considered but are not persuasive for the same reasons of record. There is no reasoning put forth to evidence that the members are not so diverse as to create an improper Markush. As previously set forth there is uncommon structure, function, effects and uses. No subject matter has been indicated allowable and there is no provision for holding the objection in abeyance.

Claim Rejections - 35 USC § 112

9. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 3-7, 9, 13 and 16-20 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

As set forth therein, applicant's claims have been amended from the generic of any disease or injury to the sub-generic of diseases and injuries "other than an autoimmune disease or neoplasm." Yet Applicant's specification does not evidence that Applicants were in possession

of the methods for the sub-generic class, nor does the specification describe this sub-generic class such that the skilled artisan is apprised of the members of the sub-genus in comparison to the genus. Thus, the recitation appears to lack adequate written description to show that Applicants were in possession of sub-genus, its inclusive and exclusive members at the time of filing. Thus, the claims lack adequate written description under 35 USC 112, first paragraph.

Applicants argue essentially as set forth for the new matter rejection. In particular applicants argue that a preferred embodiment of the invention includes treating diseases or disorders which are not autoimmune diseases or neoplasias and thus that it is clear that applicants were in possession of the sub-genus, that it is supported by the specification. Applicants contend that the written description rejection is one and the same as a new matter rejection, with reference to MPEP 2163.06.

Applicant's arguments filed 7-29-02, Paper No. 28, have been fully considered but are not persuasive. It is not agreed that within 35 USC 112, first paragraph, written description and new matter are the same, see in particular MPEP 2163 in full. While a specification may provide a description in words to support a claim limitation, it is not true that the description adequately describes the claimed subject matter. The artisan must be able to clearly understand that an applicant has invented the subject matter claimed, or that the specification describes the claimed subject matter in full to the extent that it is placed within the public's possession. While provisions within 35 USC 112, first paragraph pertain to new matter with respect to 35 USC 132, other provisions pertain to adequate description with respect to possession. The communication of the subject matter of the claims must be described in such a manner that the artisan is provided the ability of making and using the full scope of the claims. By doing so it is available to the

artisan and the public.

For example, a genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

The instant claims represent a sub-genus, methods of ameliorating the effect of injury on

the central or peripheral nervous system or the degenerative effects in the grey and/or white matter caused by a disease that results in a degenerative process, said disease being other than an autoimmune disease or a neoplasia. As in MPEP 2163, "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art."

Applicant's traversal contends that the specification in particular at p. 24, lines 14-19 would be an adequate description to convey to the artisan the subject matter claimed, including it's relevant "effects" i.e., of injury on the central or peripheral nervous system or the degenerative effects in the grey and/or white matter, and "diseases" i.e., that result in a degenerative process, said disease being other than an autoimmune disease or a neoplasia, as claimed. Such is required for the artisan to understand the members of the sub-genus, i.e., the effects and diseases, and to conclude that applicants were in possession of the full sub-genus recited in the claims.

However, neither the specification nor the art clearly delineates any litmus test whereby one can determine the relevant characteristics of the diseases or effects as claimed. The artisan is not readily apprised of those diseases of all diseases which are, "a disease that results in a degenerative process, said disease being other than an autoimmune disease or neoplasia." Similarly, the artisan is not readily apprised of those effects of all effects which are, "of injury on the central or peripheral nervous system or degenerative effects in the grey and/or white matter".

In short, the sub-genus is not adequately described such that its members are readily apparent. Consider for example that a disease such a Alzheimer's or Parkinson's which are not

generally considered to be of an autoimmune nature, have autoimmune components including activation of inflammatory cytokines, inflammatory cells and even circulating antibodies to self antigens.

Thus, neither the description nor the art clearly delineates the members of the claimed genus such that the artisan can clearly discern that applicants were in possession of the sub-genus members claimed. Therefore, the claims lack adequate written description support.

10. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 3-7, 9, 13 and 16-20 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ameliorating degenerative effects consistent with Example 9 in crush injury of rat optic nerve, ischemia and in injuries associated with ischemia as claimed in claim 3 does not reasonably provide enablement for the broad but sub-generic recitation of ameliorating the degenerative effects of injury or disease, wherein said injury or disease is other than an autoimmune disease or a neoplasm. It is noted that neuro-degenerative effects consistent with Example 9, crush injury include neuro-degenerative effects due to ischemia as crush injury is not a severing of the axonal connections in the optic nerve but yet the injury is consistent with perturbation of the blood flow to the area, i.e., ischemia.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, in particular for alternative diseases not largely associated with crush trauma or ischemia, for example glaucoma, Alzheimer's etc., as claimed in claim 4 and for example hearing loss or mental retardation.

The specification is insufficient to enable one skilled in the art to practice the invention as

broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The scope of the claims encompass amelioration of degenerative effects of injury or disease on the CNS or PNS wherein the injury or disease is other than an autoimmune disease or a neoplasm. Thus the scope encompasses at least those diseases as recited in the dependent claims not expected to be commensurate with either crush injury or ischemia including those of diabetic neuropathy, senile dementia, Alzheimer's, Parkinson's, glaucoma, Huntington's, ALS, vitamin deficiency, but also for example, hearing deficits, color blindness and mental retardation. The effects encompassed by these diseases are thus broad including for example, neuritic plaques, aberrant sugar regulation, insulin insensitivity, motor dysfunction, intraocular pressure, blurred vision, blindness, pain, sensory deficits, memory deficits and cognitive deficits, which effects are not commensurate with ischemia and crush injury.

The specifications guidance (with respect to administration of MBP) is limited to the example of crush injury of rat optic nerve and inhibition of secondary (Wallerian) degeneration as indicated by an about 1.3 greater fold number of labeled retinal ganglion cells in MBP treated animals as compared to controls. Yet the etiology and pathology of ischemia and crush injury are largely dissimilar and would not be expected by the artisan to benefit for example, diabetic neuropathy, senile dementia, Alzheimer's, Parkinson's, glaucoma, Huntington's, ALS, vitamin deficiency, hearing impairments, color-blindness or mental retardation and thus these diseases are not commensurate in scope with those degenerative effects noted for example in neuronal crush models or in ischemia.

Further, the art is unpredictable in the requirements necessary for the amelioration of degenerative effects including neuronal degeneration sufficient to restore function, see for example Liuzzi et al., Neurosurg. Clin. N.A., 2(1):31-42, 1991 with respect to peripheral nerve regeneration, Jackowski et al., Br. J. Neurosurg., 9:303-317, 1995 with respect to CNS regeneration and Morris et al., Neurology, 39:1159-65, 1989 with respect to defects/deficits associated with Alzheimer's Disease. For example, one of skill in the art would not expect a decrease in secondary (Wallerian) degeneration to be necessarily indicative or predictive of restoration of sensory and motor function, cognition or memory as encompassed by the generic claim.

Thus, the artisan is not readily assured of amelioration of the scope of effects recited in the preamble (amelioration of the (generically claimed) degenerative effects of injury or disease on the CNS or PNS, wherein the injury or disease is other than an autoimmune disease or neoplasm) without the requirement for further undue experimentation to define those effects more likely than not ameliorated in response to MBP antigen treatment.

Applicants argue that the preamble has been amended to clarify the types of effects intended to be treated. Applicants contend that the crush experiments show that the invention is efficacious for preventing or inhibiting axonal degeneration and/or promoting nerve regeneration and that accordingly the claims are not incredible. Applicants state that it is not understood that hearing impairment or color blindness is necessarily a degenerative effect on the grey and/or white matter caused by a disease that results in a degenerative process. Applicants argue that the effects or function need not be restored but merely that they can be ameliorated, ie., improved, that real world utility is established and that the artisan would not deem such effects incredible.

Applicants arguments filed 7-29-02 have been fully considered but are not persuasive. While the claims now direct that the effects to be treated are of injury on the central or peripheral nervous system or the degenerative effects in the grey and/or white matter caused by a disease that results in a degenerative process, said disease being other than an autoimmune disease or neoplasia, the clarification does not serve to clearly delineate those effects which are to be achieved or even to which diseases or injuries the effects are associated.

Applicant's arguments with respect to utility are noted. However, the rejection is not one of utility. Applicant's arguments appear to contend that as a single member within the sub-genus is enabled that the full scope of the sub-genus is enabled. However, this is not persuasive as the enablement provided by the specification must be in full scope with the claims. Hearing loss or color blindness are effects within the CNS or PNS that may result from degenerative disease. Consider hearing loss associated with repeated injury produced by loud noise, or color blindness or blindness in general associated with optic nerve damage or injury caused by a multitude of diseases including diabetes as set forth below. The loss of functional neuronal connections is a degenerative process and thus is apparently within the scope of the claim. Moreover, it is paramount that the artisan be able to discern when in fact the method claimed has been practiced. Yet providing any amelioration to the patient is not sufficient until the artisan is able to recognize such. This requires that the artisan know the relevant effects which are to be ameliorated and a suitable test whereby such can be determined. However, there does not appear to be any suitable test or guidance as to how the artisan should discern when any of the effects required have in fact been ameliorated within the full scope of the claim. Thus, for the aforementioned reasons the scope of enablement is not commensurate with the scope of the claims and therefore the scope of

enablement rejection is maintained.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 3-7, 9, 13 and 16-20 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants claim structure recites administering to a human having an injury or disease wherein the injury or disease encompasses all injuries and diseases with the exception of when the injury or disease is an autoimmune disease or neoplasm. Yet the specification fails to readily distinguish the metes and bounds of the injuries or diseases included or excluded from the claim.

While the skilled artisan recognizes several diseases which may appear to fall in one category or the other, the art recognizes multiple diseases which may be viewed as autoimmune in nature which appear to be encompassed by dependency in applicant's claims. In particular, Weiner et al., US 5,858, 364 of record recognizes a list of autoimmune diseases including diabetes and diabetic neuropathy. Thus, diabetes would appear to be excluded, yet claim 4 specifically recites diabetic neuropathy and glaucoma which are recognized as degenerative effects on the central or peripheral nervous system of diabetes, see in particular Weiner et al., column 6, lines 41-49 and Merck Manual, Yucel and Enoch, each of record. Thus, the metes and bounds of the encompassed effects, injuries and diseases appears to be indefinite as claimed. Clarification is required.

It is noted that many effects of neurodegeneration as a genus cross the sub-generic class

of diseases which may be classified as autoimmune in nature. For example, diabetes (diabetic neuropathy) may produce deficits in sensory and motor function similar to trauma, see in particular Enoch and Yucel, of record. (Alternatively, applicant's dependent claims do not further limit, but broaden).

Applicants argue that diabetic neuropathy is not an autoimmune disease and that it is not caused by an attack of the immune system on the self not withstanding the fact that it is found within diabetic patients and may be a side effect of diabetes. Applicants argue that it is beneficial to have the neuropathy or glaucoma treated even though it is secondary to their diabetes. Applicants also argue that as set forth at p. 23, line 24 to page 24, line 13, that the listed diseases such as diabetic neuropathy are not considered by the artisan to be autoimmune diseases or disorders.

Applicant's arguments filed 7-29-02 have been fully considered but are not persuasive. The arguments do not clarify the metes and bounds or scope of the claims with respect to it's recitations. The aforementioned articles clearly set forth that diabetic neuropathy is a degenerative process within the CNS or PNS and that it is mediated by autoimmune components including inflammatory cells and cytokine activation. Thus, the literature does not support the specification's conclusion that the listed diseases are not recognized by those of skill in the art as being of an autoimmune nature. Moreover, the lists are not a part of the generic claims. Neither the specification nor the art clarify any litmus test for determining whether a particular disease is of an autoimmune or neoplasia nature. Degenerative processes within the nervous system are largely recognized as being mediated by autoimmune activation, see in particular a general description of Wallerian degeneration in nerve damage mediated by activation of autoimmune

macrophages which clear cellular debris, Jackowski, of record above. Thus, the metes and bounds of the diseases and effects as encompassed by the claims remains indefinite to the artisan.

Priority

12. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Israel on 5-19-98. Applicant has filed a certified copy of the application as required by 35 U.S.C. 119(b), received as Paper No. 18, 5-16-01.

However, applicants argue in response to the 35 USC 103 rejection that priority is claimed to IL 121349 filed July 21, 1997. A certified copy of the application has not been received by the Office and more importantly applicant's Oath and Declaration does not properly claim priority or identify the priority document. Moreover, a review of the parent PCT file sets forth the decision of 12 January 2000, denying applicants right to withdraw the withdrawal of the priority claim. The authorized agent's original actions were upheld in accordance with PCT Rule 90.3 and as supported by Link v. Wabash 370 US 626, 633-34(1962). Thus the priority claim is not valid through the PCT filing. In addition, the foreign priority would not be valid in accordance with 119(a)-(d) as the relevant date of priority is more than 1 year prior to instant US filing date of 22 December 1998. Therefore priority to the IL 121349 application cannot be established.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. As set forth in the action of 10-22-02, paper No. 29 and 3-27-02, Paper No. 27, claims 3, 5-7, 9, 13, 16-17 and 19-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al., PNAS 94:10873-10878, September 1997, and The Merck Manual, Merck & Co., Inc., 1992, pp. 1510-11, 1518-23, 110-11, 412-13 and 1452-59

Becker et al., teach administration of myelin basic protein (MBP) to decrease stroke size (neuronal degeneration or to promote regeneration of CNS neurons) after transient focal cerebral ischemia. Ischemia is not deemed an autoimmune disease or neoplasm as the cause is occlusion of blood flow and not an autoimmune disease or a neoplasm. Thus, the injury or disease of ischemia is within the scope of the injuries and diseases as encompassed by the generic claim. In particular, ischemia is widely recognized in the injuries of claim 3, including blunt trauma, penetrating trauma hemorrhagic stroke, ischemic stroke and damages caused by surgery due to a lack of blood flow. Becker et al., teach administration of MBP via repetitive gavage with 1 mg of protein in 0.5 ml of PBS every 2-3 days for 2 weeks (a total of 5 feedings), and by injection with 50 ug in 50 ul of PBS with equal amounts of complete Freund's Adjuvant, see in particular,

Materials and Methods, p. 10873, column 2. The administration is deemed an effective amount as the activity reducing neuronal degeneration and/or of promoting regeneration is provided, see in particular Figures 2 and 3 wherein infarct size is reduced. The treatment ameliorates degenerative effects such as neuronal degeneration and cell death within the infarct.

Becker et al., does not specifically teach administration in humans.

However, Becker et al., does teach that other species including humans can be tolerized, see in particular Conclusions, p. 10877. Becker suggests that humans can be orally tolerized and administration of MBP to humans has been proven to be safe. Thus, Becker suggest that it is conceivable that MBP can be used to treat patients at risk of ischemia for example with cerebrovascular disease. As evidenced in the Results, Discussion and Conclusion sections, Becker et al., teach the similarity of the immunologic responses of rats to humans in response to ischemia and as recognized in the art, animal models including the rat transient focal ischemia model is used as a model to predict relative outcomes to similar pathologic injury or disease in humans.

Moreover, the Merck Manual, 1992, pp. 1510-11, 1518-23, 110-11, 412-13 and 1452-59 teach the recognition of ischemia in humans and similarity in pathology including after injury or trauma and in diseases such as stroke.

Thus, it would have been prima facie obvious to the skilled artisan that the administration of MBP to ameliorate the degenerative effects of ischemia could also be used to ameliorate degenerative effects largely due to ischemia for example in injuries and diseases including blunt trauma, penetrating trauma hemorrhagic stroke, ischemic stroke and damages caused by surgery due to a lack of blood flow. One of skill in the art would have expected positive results based on

the cumulative reference teachings of such utility as evidenced by Becker et al., and the similarity in the pathology of ischemia between rats and humans as evidenced by Becker and the Merck Manual. In addition, one of skill in the art would be motivated to administer MBP based on the beneficial results of Becker and the recognition in the art that ischemia is prevalent, if not causative in the noted neurologic diseases. One of skill in the art would have an expectation of success in such treatments as the patients rats of Becker exhibit decreased infarct size and neuronal degeneration. The artisan would clearly recognize that the patients and symptomatology coincide to each other. Thus, the reference teachings render the claimed invention drawn to the amelioration of degenerative effects obvious with respect to ischemia and the noted injuries as recited in claim 3 which are associated with ischemia.

Applicants argue that Becker is not available as prior art because of applicants' right to priority to IL 121349 filed July 21, 1997. Applicants therefore argue that Becker is not valid prior art and that the Examiner does not contend that Merck alone renders the invention obvious.

Applicant's arguments filed 7-29-02 have been fully considered but are persuasive. As discussed in the priority determination above, the Examiner is not aware of any provision whereby priority to the foreign application may now be established. Thus, Becker is valid prior art and the rejection is maintained.

Status of Claims

15. No claims are allowed.

Conclusion

16. This is a CPA of applicant's earlier Application No. 09/218,277. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
5-12-03

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